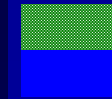


Influenza Vaccine Manufacturing

Influenza Vaccine Timeline



FDA / CDC

Manufacturing and Distribution

Jan...Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

planning & preparation

receive candidate seed viruses

prepare high-growth reassortants

monovalent concentrate production

start ↑ 1st 2nd 3rd strain

potency test reagent preparation

↑ ↑
strain selection

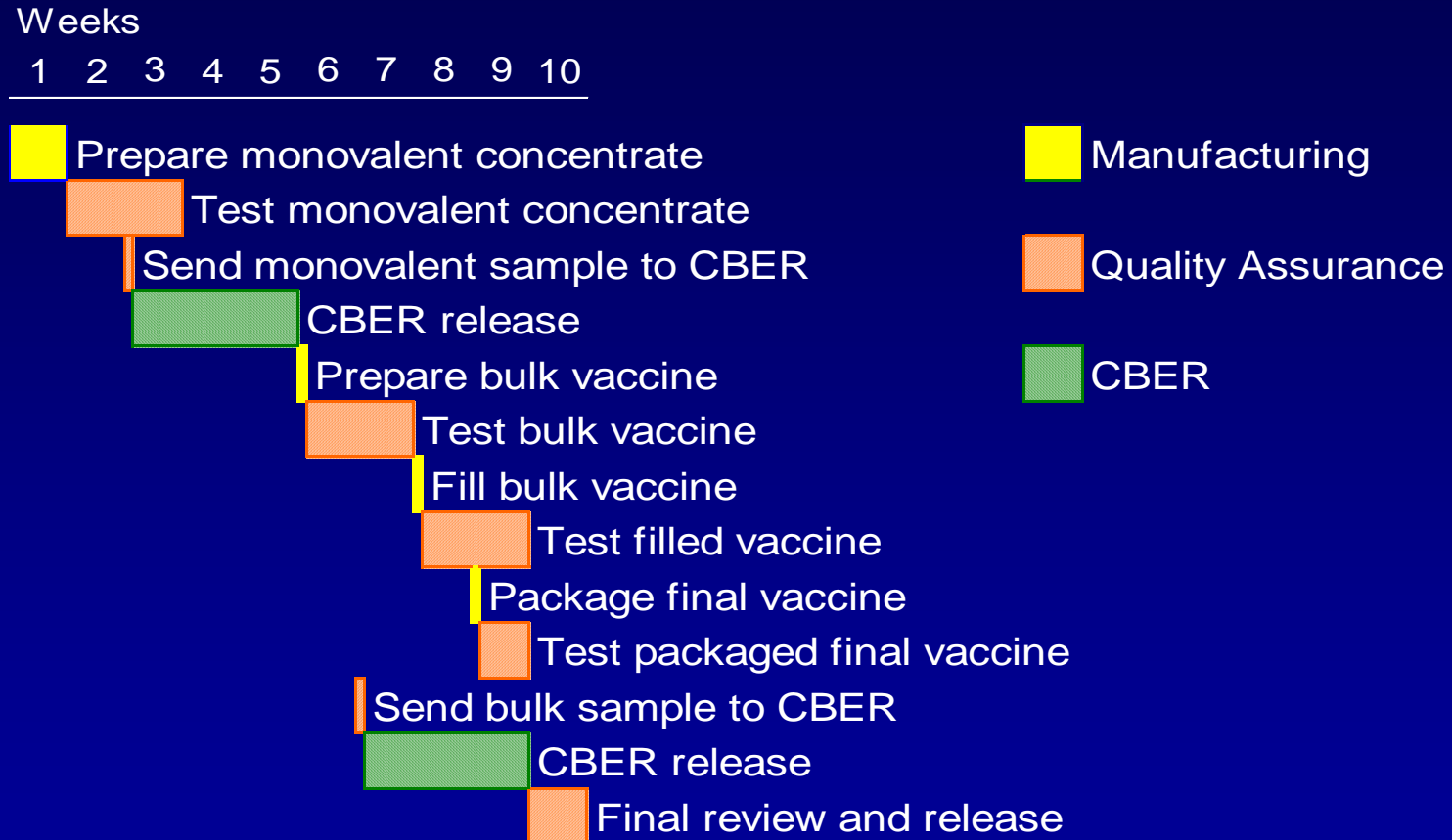
vaccine formulation

vaccine filling

↑
license issued

vaccine distributed

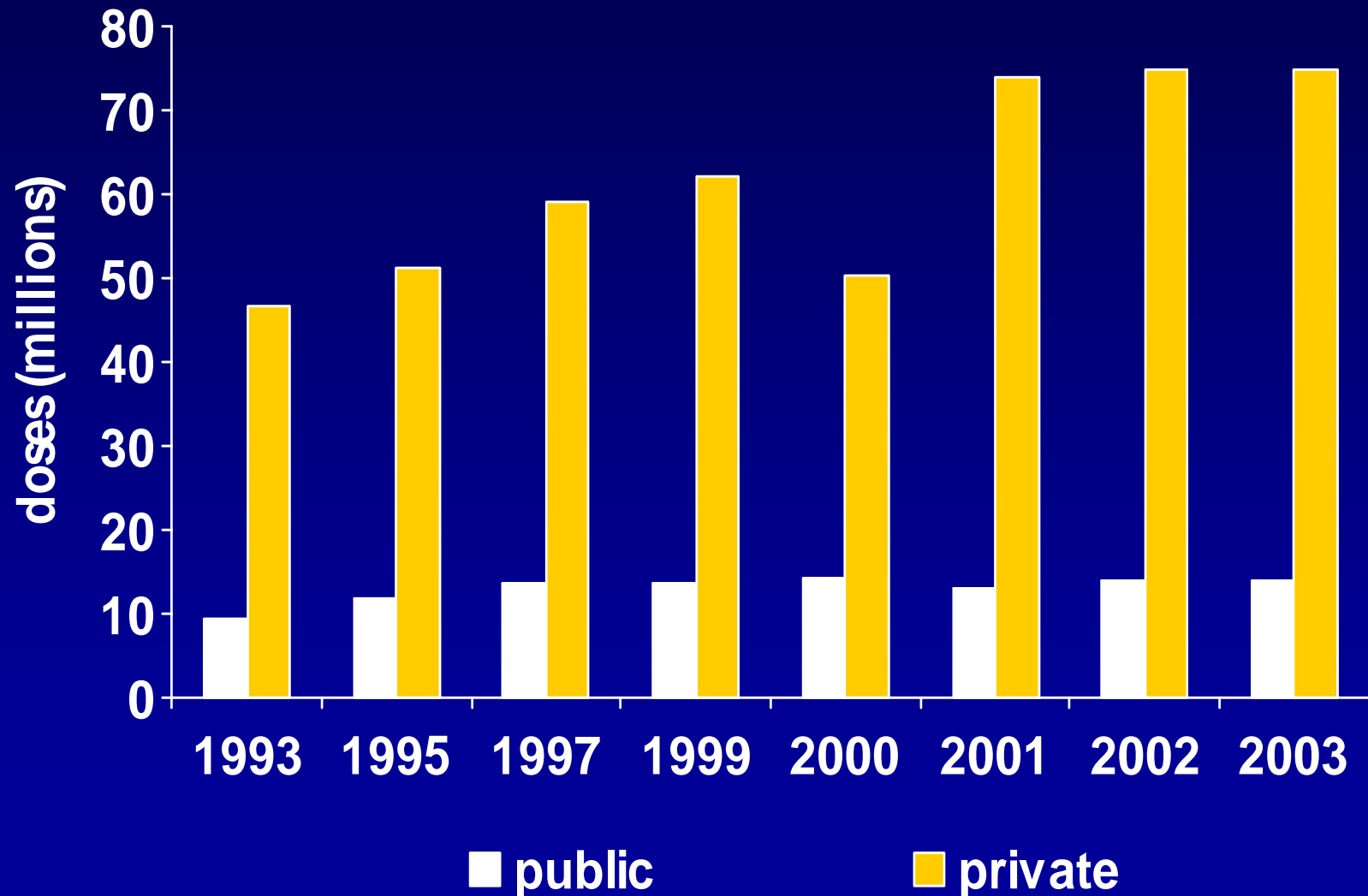
Manufacturing Timeline: Overview for One Lot



Assumptions:

- Availability of potency testing reagents
- Approved packaging components (labels, package inserts)

Distribution of Influenza Vaccine in U.S. Increased Substantially in Last Decade



Vaccine Supply / Demand

Environment: Recent Trends

- In 2002, insufficient demand resulted in manufacturers discarding 12 million doses intended for US market
- Vaccine orders in 2003 were down significantly, indicating demand would be less than in the prior season
- Production based on pre-book orders plus safety margin made at manufacturer's risk

2003-04 Season Summary

- **Apparently ample supply (83-87 M doses) existed in third quarter, 2003**
- **Early influenza outbreaks created unprecedented surge in vaccine demand late November & December, after production completed, exhausting supplies**
- **Manufacturers proactively notified CDC of late surge, worked with CDC to allocate vaccine to states, and offered remaining doses to CDC**

2004-05 Season – Key Events

- Approximately 100 million doses predicted for US
- End of August - Chiron announces vaccine delay
- Aventis Pasteur has shipped by early October approximately 33 million of planned 50 million doses
- October 5 - Chiron announces vaccine not available; ACIP and CDC create interim recommendations
- CDC and Aventis Pasteur promptly communicate to begin situation assessment and develop action plan
- Aventis Pasteur increases production to total of 58 million doses of vaccine for 2004-2005 season
- In coordination with CDC's distribution plan, Aventis Pasteur ships vaccine to prioritized customers

Influenza Vaccine: Key Lessons, Recommendations

Influenza Vaccine: Key Lessons

- **Consistent increases in demand drive:**
 - Increased vaccine supply
 - Improved vaccine distribution & administration capabilities
- **Clear, consistent and authoritative recommendations drive increased demand over time**

Recommendations Concerning Influenza Vaccine and Vaccination

- **Raise vaccination rates**
 - Promote provider and consumer education about influenza immunization recommendations
 - Urge health care workers to set an example by being vaccinated
 - Develop innovative and sustainable initiatives to drive demand
- **Expand vaccination recommendations incrementally to include larger proportion of population**

Vaccine Manufacturing: Challenges and Opportunities

Challenges for Vaccine Manufacturers

- **Biological organisms not always predictable**
- **Stringent regulatory requirements**
- **Substantial, ongoing & increasing costs:**
 - R & D
 - Regulatory compliance
 - Facilities
 - Skilled workforce
- **Unique, increasing liability concerns**
- **Dramatic impact of policy changes**
- **Undervaluation of vaccination**

Recommendations for Improving Vaccine Manufacturing Environment

- **Improve FDA resources & surge capacity to meet increasing demands**
- **Recognize impact of vaccine pricing on supply & on manufacturing capacity**
- **Ensure adequate, fair reimbursement for vaccines & for vaccine administration**
- **Strengthen the Vaccine Injury Compensation Program**
- **Involve vaccine manufacturers at earliest & all stages of policy discussions**